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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/682,662

10/09/2003

Sinan Tas

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EXAMINER

ANDERSON, JAMES D

ART UNIT

PAPER NUMBER

1614

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DELIVERY MODE

05/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/682,662	Applicant(s) TAS ET AL.	
	Examiner JAMES D. ANDERSON	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32,34 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32,34 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☐ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) ☒ Other: <u>Color Drawings Petition Decision</u> . |

DETAILED ACTION

Claims 32, 34, and 36 are presented for examination

Applicants' amendment filed 3/27/2008 has been received and entered into the application. Accordingly, claims 32, 34, and 36 have been amended and claims 1, 8-9, 11, 27-28, 31, 33, 35, and 37-52 have been cancelled.

Applicants' arguments have been fully considered and are persuasive in view of the cancellation of all previously rejected claims. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

In light of the new rejections being applied against the pending claims, the finality of the previous Office Action is hereby *withdrawn* and prosecution is reopened. This Office Action is **Non-Final**.

Reasons for Reopening Prosecution

In the first Office Action mailed 9/14/2006, USP No. 6,432,970 to Beachy *et al.* was applied as 102(e) prior art against the claims. Applicants persuasively argued in their reply filed 2/16/2007 that Beachy *et al.* does not anticipate the then rejected claims and the rejection over Beachy *et al.* was withdrawn. However, upon further consideration of the Beachy *et al.* disclosure, the Examiner is herein applying Beachy *et al.* as a prior art reference under 35 U.S.C. 103 in view of the recent decision in *KSR vs. Teleflex*. Beachy *et al.* clearly suggest that a compound such as cycloamine can be used to treat psoriasis. As such, it is well within the

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purview of the skilled artisan to try different doses of cyclopamine until the desired effect is achieved (in this case, treatment of psoriasis). While it is certainly true that Beachy et al. discuss the modulation or treatment of numerous human pathologies, the fact remains that the reference exemplifies psoriasis, wherein Beachy et al. explicitly indicate psoriasis as a proliferative skin disorder encompassed by the disclosure (col. 10, line 63 to col. 11, line 1), define what is meant by the term psoriasis (col. 11, lines 37-49), and explicitly discuss the treatment of psoriasis with a preparation of the invention (col. 41, lines 36-57). Beachy et al. also acknowledge the fact that hedgehog antagonists can be inductive or anti-inductive with respect to proliferation or differentiation of a given tissue (col. 29, lines 45-47). As such, the Examiner is not persuaded by Applicants' arguments that Beachy et al. is ambiguous with respect to the effects of the claimed compounds because Beachy et al. acknowledge and discuss the fact that the compounds of the invention can have different effects in different tissues. However, the fact remains that Beachy et al. explicitly suggest and motivate one skilled in the art to use a hedgehog antagonist (e.g., cyclopamine) to treat psoriasis.

In addition to their arguments in the reply filed 2/16/2007, Applicants also amended claim 1 and submitted new claims with the limitation "in a sufficient amount that induces differentiation of epidermal cells in lesional skin and the regression and/or disappearance of said skin lesions" (see present claims 32 and 34). In addition, a newly added claim (claim 27) introduced the limitation "in a sufficient quantity to provide, within 8 days of administration, an average of 80% or greater decrease in the severity of psoriatic lesions, taking into account the elevation from skin surface, erythema and scaling of the lesions". Upon careful review of the specification and original claims, the Examiner is unable to find support for these claim

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limitations. With respect to dosages and amounts of cyclopamine, Applicants disclose concentrations of 0.001 mM to 100 mM, preferably 9 mM to 24 mM (page 15, lines 14-18). However, nowhere do Applicants describe administering to a psoriasis patient cyclopamine in a "sufficient amount that induces differentiation of epidermal cells in lesional skin and the regression and/or disappearance of said skin lesions" or "in a sufficient quantity to provide, within 8 days of administration, an average of 80% or greater decrease in the severity of psoriatic lesions, taking into account the elevation from skin surface, erythema and scaling of the lesions", other than those specific doses that were administered to patients in the examples. Accordingly, claims 32, 34, and 36 are newly rejected under 35 U.S.C. 112, 1st Paragraph (New Matter).

Petition to Submit Color Photographs

Per the attached Petition Decision, the petition to submit color photographs filed 10/9/2003 is GRANTED.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 34, and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

In the reply filed 2/16/2007, Applicants amended claim 1 and submitted new claims with the limitation "in a sufficient amount that induces differentiation of epidermal cells in lesional skin and the regression and/or disappearance of said skin lesions" (see present claims 32 and 34). In addition, a newly added claim (claim 27) introduced the limitation "in a sufficient quantity to provide, within 8 days of administration, an average of 80% or greater decrease in the severity of psoriatic lesions, taking into account the elevation from skin surface, erythema and scaling of the lesions" (see present claim 36).

Upon careful review of the specification and original claims, the Examiner is unable to find support for these claim limitations. With respect to dosages and amounts of cyclopamine, Applicants disclose concentrations of 0.001 mM to 100 mM, preferably 9 mM to 24 mM (page 15, lines 14-18). In relation to these broad doses, Applicants do not mention induction of differentiation of epidermal cells in lesional skin and the regression and/or disappearance of said skin lesions or an average of 80% or greater decrease in the severity of psoriatic lesions, taking into account the elevation from skin surface, erythema and scaling of the lesions. Further, nowhere do Applicants broadly describe administering to a psoriasis patient cyclopamine in a "sufficient amount that induces differentiation of epidermal cells in lesional skin and the regression and/or disappearance of said skin lesions" or "in a sufficient quantity to provide, within 8 days of administration, an average of 80% or greater decrease in the severity of psoriatic lesions, taking into account the elevation from skin surface, erythema and scaling of the lesions", other than those specific doses that were administered to patients in the examples.

Accordingly, claims 32, 34, and 36 contain limitations that are deemed to be new matter submitted in the response filed 2/16/2007.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32, 34, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over USP No. 6,432,070 (Issued Aug. 13, 2002; Filed June 4, 1998) ("Beachy *et al.*").

The prior art discloses treating various disorders "associated with" abnormal epidermal cell proliferation/differentiation, and especially psoriasis (column 11, lines 35- 49), by inducing differentiation of epidermal cells (column 41, lines 43-57) with a steroidal alkaloid hedgehog antagonist, *e.g.*, cyclopamine (Figure 1; column 19, lines 40 and 41). Additional steroids can be co-administered therewith, *e.g.*, hydrocortisone (column 28, lines 40-55). Beachy *et al.*

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explicitly indicate psoriasis as a proliferative skin disorder encompassed by the disclosure (col. 10, line 63 to col. 11, line 1), define what is meant by the term psoriasis (col. 11, lines 37-49), and explicitly discuss the treatment of psoriasis with a preparation of the invention (col. 41, lines 36-57). Beachy *et al.* also acknowledge the fact that hedgehog antagonists can be inductive or anti-inductive with respect to proliferation or differentiation of a given tissue (col. 29, lines 45-47).

The prior art states that an "effective amount" of hedgehog antagonist is that which brings about "a change in the rate of cell proliferation and/or the state of differentiation of a cell" (col. 9, lines 8-15). Patentees are silent regarding the particular differentiation-related dosing recitations of instant claims 32 and 34, but the state of the prior art is such that they would reasonably be expected to naturally occur when cyclopamine is administered in an effective amount to a patient having psoriasis as suggested and motivated by Beachy *et al.* Furthermore, with regard to instant claim 36, which is not specific to differentiation inducing doses, all that is required is even a minor "decrease" in severity of psoriatic lesions to meet the limitations of those claims as currently constructed. Thus, any "effective" therapy would be expected to exhibit sufficient symptomatic relief to fall with the metes and bounds of those claims.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer cyclopamine to a patient having psoriasis. Beachy *et al.* explicitly contemplate and suggest such a treatment method and the recent decision in *KSR vs. Teleflex* supports rejections over prior art where there are a finite number of predictable solutions. In such cases, it is not deemed an act of invention to try different embodiments of the prior art treatment methods to determine which one works best when Beachy *et al.* clearly

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suggest that compounds of the invention are useful for treating psoriasis. For example, Beachy *et al.* exemplify the treatment of psoriasis with a compound of the invention and further exemplify cyclopamine as a compound of the invention. As such, it would take no more than routine experimentation to administer different doses of cyclopamine to patients having psoriasis in order to determine a therapeutically effective dose given the teachings of Beachy *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

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